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A computerized model based on Bayes' theorem was designed to predict whether bronchogenic cancer could be resected for cure. Beginning 1 January, 1986, 100 consecutive patients undergoing thoracotomy for suspected lung cancer were prospectively analyzed. Eighty-five patients were found to have bronchogenic cancer and the remaining 15 were excluded from the study. Thirty-three risk factors were used to characterize the patient population. Bayesian conditional probabilities were derived from literature values and physician estimates.

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Theoretical Surgery

A predictive model of resectability for patients with bronchogenic carcinoma*

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Abstract. A computerized model based on Bayes' theorem was designed to predict whether bronchogenic cancer could be resected for cure. Beginning 1 January, 1986, 100 consecutive patients undergoing thoracotomy for suspected lung cancer were prospectively analyzed. Eighty-five patients were found to have bronchogenic cancer and the remaining 15 were excluded from the study. Thirty-three risk factors were used to characterize the patient population. Bayesian conditional probabilities were derived from literature values and physician estimates. Each of the 85 patients was prospectively evaluated by the Bayesian model to predict the probability that the lesion would be unresectable. These predicted results were then compared with observed results:

Predicted probability of unresectable cancer	Observed unresectable cancer
5%	3% (1/37)
5%-50%	19% (7/38)
50%-80%	71% (5/7)
80%	100% (3/3)
95%	100% (1/1)

Bayesian theory can be used to generate a reliable model of resectability in patients with bronchogenic cancer. The results may have practical application in decision-making support systems that address the management of patients with pulmonary neoplasia.

Key words: Bayesian theory – Cancer – Pulmonary

Introduction

The patient with suspected bronchial cancer often poses a difficult management problem. Decision theory has been used to provide a basis for recommending either expectant management, surgery, or biopsy. Kunstaetter et al. [5] have described a logical, organized approach to this clinical problem by presenting a decision tree based on probability estimates obtained from the literature. The majority of these probabilities can be obtained from published reports, but there is a paucity of information regarding the resectability of pulmonary lesions.

The probability that bronchogenic cancer can be "resected for cure" is one of the more important factors in the decision- making process. Unfortunately, this probability is dependent on multiple factors that have not been well defined. The problem is made more complex because of the fact that the criteria for resectability may vary from one institution to another. Also, in recent years, there has been a gradual trend toward more aggressive surgical therapy [6]. Selected patients having mediastinal lymphatic involvement are now offered operation, whereas only a few years ago they would have been considered unresectable. Clearly, the estimatation of this probability depends

* The opinions or assertions contained herein are the privat views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense

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on a variety of clinical and radiographic measurements that must be specific for each individual patient.

These problems can be minimized by using a Bayesian statistical model to predict the probability that a given pulmonary cancer will be resectable. We have devised such a model based on a retrospective review of patients undergoing thoracotomy for bronchogenic carcinoma at our hospital. Our results indicate that this approach offers a sound basis for predicting the resectability of malignant pulmonary lesions.

Theory

Bayesian statistical theory predicts the probability of future events based on the characteristics of prior associated events. This predictive ability is usually put to practical advantage by considering the "events" to be diagnostic categories [1, 3, 8]. As pointed out recently by DeDombal [2], these categories may be prognostic rather than diagnostic. In this context, Bayesian analysis allows one to make prognostic predictions based on the known clinical behavior of previously evaluated patients.

A large number of variables usually produces a Bayesian algorithum that is best handled by a computer. Information gained from previously evaluated patients is stored in the computer as a matrix of conditional probabilities. This conditional probability matrix (CPM) is then used by the Bayesian mathematical algorithm to calculate the probability of each prognostic or diagnostic category.

The CPM consists of a number of patient observation and the frequency with which those observations are found in a given category. The frequency of these risk factors is best determined from a retrospective study of the selected patient population. After the CPM has been generated, it may be incorporated into a computer program for subsequent use by the Bayesian algorithm. Recently we presented a step-by-step approach that should provide specific guidance to those interested in developing Bayesian studies [4].

Patients and methods

From 1 January 1986 through 26 March 1987, we obtained clinical records and radiographs on 100 consecutive patients undergoing thoracotomy for pulmonary parenchymal lesions. The diagnosis for each patient was confirmed by histological examination. Fifteen patients were found to have benign lesions and were not included in the study. The remaining 85 patients had bronchogenic cancer.

Table 1. Preoperative patient parameters

Clinical findings	
1	Age (< 45; > 45)
2	Sex
3	Smoking history
4	Weight loss
5	Hemoptysis
6	Cough
7	Chest pain
8	Complaints consistent with hypertrophic osteoarthropathy
9	Bloody pleural effusion
10	Previous cancer
Radiographic findings	
11	Size of lesion (< 3; 3–6; > 6 cm)
12	Change in size
13	Margins of lesion (smooth; irregular)
14	Calcification
15	Homogeneity
16	Cavitation
17	Pleural effusion
18	Bilateral lesions
19	Multiple lesions
20	Lobulation
21	Spiculation
22	Middle lobe lesion
23	Tracheal deviation
24	Distal atelectasis
25	Chest wall abutment
26	Chest wall invasion
27	Mediastinal abutment
28	Hilar nodal enlargement
29	Mediastinal nodal enlargement
Bronchoscopic findings	
30	No endobronchial lesions
31	Endobronchial lesion seen
32	Extrinsic compression
33	Blunted carina

Our criteria for resectability followed well-accepted guidelines [7]. We considered lesions to be "resectable for cure" if the pulmonary malignancy could be completely removed and mediastinal involvement, if any, was limited to ipsilateral intranodal disease. Patients found to have mediastinal involvement on mediastinoscopy or anterior mediastinotomy were not included in this study.

We devised a computerized predictive model based on the Theorem of Bayes. The model was set up to categorize the patients as either "resectable" or "nonresectable". A total of 33 patient factors were selected to preoperatively characterize the population (Table 1). We sought to choose those features that were apt

Table 2. Patient characteristics

Age < 45	10 (12%)
Age < 45	75 (88%)
Male	61 (72%)
Female	24 (28%)
Smoking history	81 (84%)
Weight loss	13 (15%)
Hemoptysis	19 (22%)
Chest pain	13 (15%)
Pleural effusion	0
Calcification	0
Size of lesion	
< 3 cm	28 (33%)
3–5 cm	40 (47%)
> 5 cm	17 (20%)
Margin of lesion	
Smooth	7 (8%)
Minimally irregular	42 (50%)
Very irregular	36 (42%)
Radiographic evidence of	
N1 disease	11 (13%)
N2 disease	16 (19%)
Chest wall involvement	19 (22%)
Multiple lesions	7 (8%)

to discriminate resectable from non-resectable lesions. Unfortunately, such characteristics have not been well defined in the literature, and we were therefore quite liberal in the selection process. There is no penalty for chossing a factor that does not discriminate well, since such a factor will be associated with conditional probabilities that are approximately equal for each category, thereby having a minimal effect on the final results.

The conditional probabilities were based on physician estimates and a retrospective review of similar patients undergoing thoracotomy for pulmonary parenchymal lesions. The prior probabilities were assumed to be the frequency with which each category ("resectable" or "non-resectable") had occurred. The technique for deriving the CPM has been covered in detail elsewhere [1, 4]. Generally, we used the retrospective review for the CPM values, but physician estimates were necessary when there was insufficient documentation.

A computer program was written to use these conditional and prior probabilities in a Bayesian algorithm. Each of the 85 patients with malignant disease was entered into the program, and the model calculated the probability that each lesion would be unresectable. A clinical profile of these 85 patients is given in Table 2.

Table 3. Predicted and observed rate of unresectability

Computer-predicted probability of unresectable disease (%)	Actual outcome		
	Resectable	Non-resectable	Unresectable (%)
< 5	36	1	3
5–50	31	7	19
50–80	2	5	71
> 80	0	3	100
> 95	0	1	100

Results

Of the 85 patients with malignant disease, 16 were found to be unresectable. The majority of these unresectable patients had malignant invasion of mediastinal structures to include the heart, great vessels, and esophagus. Other reasons for unresectability in this group included involvement of the main stem bronchus within 2 cm of the carina, high extranodal paratracheal lymph-node metastasis, proximal involvement of the pulmonary artery, and diffuse intrathoracic metastatic disease. We did not consider chest wall invasion to be a contraindication to curative resection. Four patients underwent an en bloc chest wall resection along with a lobectomy, and all were considered resectable for cure. Two of these four had postoperative radiation therapy, but no patients in the entire group received any form of preoperative adjuvant therapy.

In order to compare the predictions with actual results, we calculated the Bayesian probability that each lesion would be unresectable. We then grouped the patients as shown in Table 3 and compared our predicted rate of unresectable disease with the rate that was actually observed. For example, of the 37 patients predicted to have less [illegible] a 5% chance of being unresectable, in fact 2.7% [illegible] were actually unresectable for cure.

The interval breakdown was selected to place the patients into general risk categories. The breakdown is completely arbitrary, but does categorize patients into "low risk", "high risk", and several intermediate risk groups. Potential users may designate the intervals most appropriate to their specific application.

Discussion

Decision analysis offers an organized framework for patient management, but it suffers several limitations. Certainly one of the major problems is the data base used to define decision-tree nodal probabilities.

Whereas some of these probabilities may be well defined, more often it is quite difficult to arrive at an accurate probability estimate [9].

Different reported series may contain conflicting information, and there may be significant differences in the patient populations that are examined. In addition, there may be important differences in the management of patients from one institution to another. Perhaps a more aggressive surgical team would have resected some of the lesions we considered unresectable, while others might have elected to palliate lesions that we resected for cure. The problem is further complicated by the fact that patient management strategies change with time, thereby diminishing the reliability of older published reports. Finally, it is certainly suboptimal to extrapolate information reported on groups of patients and apply that information directly to an individual patient.

Bayesian statistical theory can circumvent most of these problems. It is possible to define the desired patient population precisely and then use a retrospective study to develop a CPM that is tailored to one's specific practice [1–4]. This will effectively eliminate the problem associated with institutional variation. Furthermore, this CPM can be periodically updated so as to obviate problems associated with management strategies that change with time. Perhaps most importantly, a predictive model generated along these guidelines provides the capability to individualize probability calculations. DeDombal [2] has recently emphasized the importance of individualized analysis and has elaborated on the advantages of Bayesian theory in this context.

It should be emphasized that the CPM determines the accuracy of the model. Generally, the CPM is regarded as a data bank of previous clinical experience [4]. Likewise, there are some advantages associated with the use of a prospective survey to derive the CPM, but the majority of published studies use retrospective studies with good results [1–4, 8].

We have demonstrated the use of Bayesian theory to generate a reliable model of resectability in patients with bronchogenic cancer. This study illustrates a previously unreported application of Bayesian analysis that may have sound practical application in decision-making support systems dealing with the management of bronchogenic tumors.

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Theoretical Surgery

Discussion forum

Anaesthetic or surgical risk?

Discussion about a protocol of a controlled clinical trial: Induction of anaesthesia and perioperative risk [Theor Surg (1988) 3:55–77]

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Key words: Protocol – Controlled clinical trial – Surgical risk – Anaesthetic risk

It has been an intensive but very rewarding task to read this detailed protocol.

Is it worth publishing a very long protocol of a controlled clinical trial?

The first question I wish to address is, have the authors established their case that it is worth publishing, in a journal of *Theoretical Surgery*, a very long protocol like this. After all, they make the point themselves that such publications are rare except in journals specifically devoted to clinical trials. My own view is that *Theoretical Surgery* proclaims in its subtitle that it is concerned with decision making, and it is therefore not only acceptable, but also desirable, that full details should be made available about the structure and planning of a large and complicated trial such as this.

The fact is that the *principles* as distinct from the *details* of all clinical trials do not vary from one to another, but it is only when one thinks about a very complicated trial like the present one that one is forced to take into account considerations that might not have even been thought of in an apparently much simpler study. How was one to ensure that the observer did not know whether Haemaccel or Ringer's solution had been infused before the operation? The authors refused to accept that it would be impossible to blind the observer, and devised a neat and ingenious technique intended to achieve this end. However, not satisfied that the technique was meant to achieve this end, they have also taken steps to find out whether they have succeeded in this aim: they have asked the observer to guess which infusate was given to each patient, so that subsequent analysis of the accuracy of the guesses would reveal whether the guesses were truly random or whether the blinding procedure had failed. The standard description of the study would have included some such phrase as "the observer did not know whether the infusate was Haemaccel or Ringer's" and the reader might well have been left in a state of critical disbelief since it would be obvious from the conduct of the trial that observer must have been present when the infusion was started and stopped and while it was running. The insistence on testing the efficacy of the blinding procedure reminds one that it is not enough to take some precaution that is aimed at eliminating an error. It is also crucial to test whether the error has been eliminated.

Another important example of attention to detail that I suspect many published trials have only paid lip-service to is the manner of patient selection. The trouble the authors have taken to make their patient groups as truly comparable as possible is an object lesson to all of us associated with clinical trials. One cannot remind oneself too often that the admirable and powerful (and sometimes very complicated) statistical tests what we use on our results are all based on the premise that the control and treatment groups differ only in the treatment they have received, but are identical in *every* other way.

If we accept that *Theoretical Surgery* should at least sometimes publish detailed protocols like this, there remains the question, how often? Naturally,